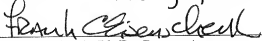


I hereby certify that this correspondence is being electronically filed in the United States Patent and Trademark Office on July 30, 2009.

  
Frank C. Eisenschek, Ph.D., Patent Attorney

REQUEST FOR CERTIFICATE OF  
CORRECTION UNDER 37 CFR 1.322  
AND UNDER 37 CFR 1.323  
Docket No. ARS.106

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Amanda Proudfoot, Marie Kosco-Vilbois  
Issued : June 2, 2009  
Patent No. : 7,541,435  
Conf. No. : 6045  
For : Antagonists of CXCR3-Binding CXC Chemokines

Mail Stop Certificate of Corrections Branch  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

REQUEST FOR CERTIFICATE OF CORRECTION  
UNDER 37 CFR 1.322 (OFFICE MISTAKE) AND  
UNDER 37 CFR 1.323 (APPLICANT MISTAKE)

Sir:

A Certificate of Correction for the above-identified patent has been prepared and is attached hereto.

In the left-hand column below is the column and line number where errors occurred in the patent. In the right-hand column is the page and line number in the application where the correct information appears.

Patent Reads:

Column 2, line 30:

“tuberculosis”

Application Should Read:

Page 3, line 14:

--tuberculosis--

Column 3, line 52:

“established that is not possible”

Column 4, lines 13-14:

“mutants having not only have a considerably”

**Patent Reads:**

Column 5, line 4:

“pico microMolar”

**Patent Reads:**

Column 6, line 25:

“to Alanine”

Column 6, line 30:

“substituted to”

Column 6, line 43:

“substituted to”

Column 6, line 49:

“substituted to”

Column 6, line 67:

“substituted to”

Column 7, lines 41-42:

“of some of basic”

Column 7, lines 44-45:

“of these group of chemokines”

Page 6, line 4:

--established that it is not possible--

Page 6, lines 23-24:

--mutants having not only a considerably--

**Application Reads:**

Page 8, line 17:

--pico -/microMolar--

**Application Should Read:**

Page 11, line 7:

--with Alanine--

Page 11, line 11:

--substituted with--

Page 11, line 21:

--substituted with--

Page 11, line 25:

--substituted with--

Page 12, line 11:

--substituted with--

Page 13, line 16:

--of some of the basic--

Page 13, line 18:

--of these chemokines--

Column 8, line 66:

“or im proving”

**Patent Reads:**

Column 9, line 17:

“proteinsu”

**Patent Reads:**

Column 10, line 34:

“compounds of present invention”

Column 12, line 8:

“Many books and reviews provides”

Column 12, line 40:

“derived form viral”

Column 15, line 2:

“to which is administered”

Column 15, lines 60-61:

“the desiredr results”

**Patent Reads:**

Column 22, Table III:

“CXCLII-WT  
CXCLII-1B3  
CXCLII-2B3”

Column 23, Table III cont.:

“CXCLII-3B3  
CXCLII-4B4”

Page 16, line 6:

--or improving--

**Application Reads:**

Page 16, line 18:

--proteins”--

**Application Should Read:**

Page 19, lines 3-4:

--compounds of the present invention--

Page 22, lines 5-6:

--Many books and reviews provide--

Page 23, line 3:

--derived from viral--

Page 27, line 21:

--to which it is administered--

Page 29, line 13:

--the desired results--

**Application Reads:**

Page 43, Table III:

--CXCL11-WT  
CXCL11-1B3  
CXCL11-2B3--

Page 43, Table III:

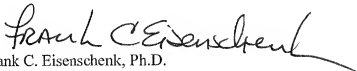
--CXCL11-3B3  
CXCL11-4B4--.

A true and correct copy of pages 8, 16, and 43 of the specification as filed which support Applicants' assertion of the errors on the part of the Patent Office accompanies this Certificate of Correction.

The fee of \$100.00 was paid at the time this Request was filed. The Commissioner is also authorized to charge any additional fees as required under 37 CFR 1.20(a) to Deposit Account No. 19-0065.

Approval of the Certificate of Correction is respectfully requested.

Respectfully submitted,



Frank C. Eisenschenk, Ph.D.

Patent Attorney

Registration No. 45,332

Phone No.: 352-375-8100

Fax No.: 352-372-5800

Address: P.O. Box 142950  
Gainesville, FL 32614-2950

FCE/jb/sl

Attachments: Copy of pages 8, 16, and 43 of the specification

59, 62, 66, 67, 70 and 71). The other basic residues of human CXCL11, and all the basic residues in mouse CXCL11, human CXCL10, and human CXCL9 are underlined. Cysteines and basic residues conserved amongst human CXCR3-binding CXC chemokines are indicated in the boxed line below the alignment, respectively, as C and B. The numbering is based on the mature human sequences, which lack a signal peptide including the N-terminal 21 (mCXCL11, hCXCL11 and hCXCL10) or 22 (hCXCL9) amino acids. The mature form of mCXCL11, hCXCL11, and hCXCL10 is shown entirely, whilst the mature form of hCXCL9 has 25 more amino acids at the carboxyl-terminus.

Figure 2: graph representing the results of the heparin-binding assay performed with [<sup>3</sup>H]-heparin, comparing the activity of CXCL11-WT and of the indicated CXCL11 mutants in microMolar range.

Figure 3: graph representing the results of the equilibrium competition receptor binding assay performed by monitoring the percentage of [<sup>125</sup>I]-CXCL11 displaced from membranes of CXCR3-expressing HEK cells, following the addition of CXCL11-WT and of the indicated CXCL11 mutants in the pico-/microMolar concentration range.

Figure 4: graph representing the results of the chemotaxis assay performed on CXCR3-expressing L1.2 cells using CXCL11-WT or the indicated CXCL11 mutants.

Figure 5: graph summarizing the results of the peritoneal cell recruitment assay, performed in Female Balb/C mice using CXCL11-WT or the other indicated CXCL11 mutants, compared to a control with saline buffer. The level of statistical significance is represented with the number of asterisks.

A second class of alternative molecules of the invention is represented by antagonists of CXCR3-binding CXC chemokines comprising one of the amino acid sequences as defined above and an amino acid sequence belonging to a protein sequence other than the corresponding CXCR3-binding CXC chemokine. This heterologous latter sequence should provide additional properties without impairing significantly the antagonistic activity, or improving GAG-binding properties. Examples of such additional properties are an easier purification procedure, a longer lasting half-life in body fluids, an additional binding moiety, the maturation by means of an endoproteolytic digestion, or extracellular localization. This latter feature is of particular importance for defining a specific group of fusion or chimeric proteins included in the above definition since it allows the molecules defined as CXCR3-binding CXC chemokines antagonists in this patent application to be localized in the space where not only where the isolation and purification of these polypeptides is facilitated, but also where CXCR3-binding CXC chemokines and their receptor naturally interact.

Design of the moieties, ligands, and linkers, as well methods and strategies for the construction, purification, detection and use of fusion proteins are widely discussed in the literature (Nilsson J et al., 1997; "Applications of chimeric genes and hybrid proteins" Methods Enzymol. Vol. 326-328, Academic Press, 2000; WO 01/77137). Additional protein sequences which can be used to generate the antagonists of the present invention are chosen amongst extracellular domains of membrane-bound protein, immunoglobulin constant region, multimerization domains, extracellular proteins, signal peptide-containing proteins, export signal-containing proteins. The choice of one or more of these sequences to be fused to the GAG-binding defective mutant of CXCR3-binding CXC chemokine is functional to specific use and/or purification protocol of said agent.

TABLE III

Protein	Heparin Chromatography		Mono S Chromatography		Difference between Heparin and MonoS [NaCl]
	Eluting concentration [NaCl]	Difference from CXCL11-WT [NaCl]	Eluting concentration [NaCl]	Difference from CXCL11-WT [NaCl]	
CXCL11-WT	0.77 M	-	1.08 M	-	-0.31 M
CXCL11-1B3	0.72 M	0.05 M	0.85 M	0.23 M	-0.18 M
CXCL11-2B3	0.64 M	0.13 M	0.97 M	0.11 M	0.02 M
CXCL11-3B3	0.44 M	0.33 M	0.85 M	0.23 M	0.10 M
CXCL11-4B4	0.62 M	0.15 M	1.14 M	-0.06 M	0.22 M

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,541,435

Page 1 of 3

APPLICATION NO.: 10/517,726

DATED : June 2, 2009

INVENTORS : Amanda Proudfoot, Marie Kosco-Vilbois

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 2,

Line 30, "tuberculosis" should read --tuberculosis--.

Column 3,

Line 52, "established that is not possible" should read --established that it is not possible--.

Column 4,

Lines 13-14, "mutants having not only have a considerably" should read  
--mutants having not only a considerably--.

Column 5,

Line 4, "pico microMolar" should read --pico -/microMolar--.

Column 6,

Line 25, "to Alanine" should read --with Alanine--.  
Line 30, "substituted to" should read --substituted with--.  
Line 43, "substituted to" should read --substituted with--.  
Line 49, "substituted to" should read --substituted with--.  
Line 67, "substituted to" should read --substituted with--.

MAILING ADDRESS OF SENDER:

Saliwanchik, Lloyd & Saliwanchik

P.O. Box 142950

Gainesville, FL 32614-2950



UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,541,435

Page 2 of 3

APPLICATION NO.: 10/517,726

DATED : June 2, 2009

INVENTORS : Amanda Proudfoot, Marie Kosco-Vilbois

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 7,

Lines 41-42, "of some of basic" should read --of some of the basic--.

Lines 44-45, "of these group of chemokines" should read --of these chemokines--.

Column 8,

Line 66, "or im proving" should read --or improving--.

Column 9,

Line 17, "proteinsu" should read --proteins"--.

Column 10,

Line 34, "compounds of present invention" should read  
--compounds of the present invention--.

Column 12,

Line 8, "Many books and reviews provides" should read  
--Many books and reviews provide--.

Line 40, "dcrived form viral" should read --derived from viral--.

Column 15,

Line 2, "to which is administered" should read --to which it is administered--.  
Lines 60-61, "thc desiredr results" --the desired results--.

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO : 7,541,435

Page 3 of 3

APPLICATION NO.: 10/517,726

DATED : June 2, 2009

INVENTORS : Amanda Proudfoot, Marie Kosco-Vilbois

It is certified that errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 22,

Table III, "CXCLII-WT	should read	--CXCL11-WT
CXCLII-1B3		CXCL11-1B3
CXCLII-2B3"		CXCL11-2B3--.

Column 23,

Table III, "CXCLII-3B3	should read	--CXCL11-3B3
CXCLII-4B4"		CXCL11-4B4--.

MAILING ADDRESS OF SENDER:  
Saliwanchik, Lloyd & Saliwanchik  
P.O. Box 142950  
Gainesville, FL 32614-2950